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Frequency of Neuropathic Pain and its Effect on Disability in Patients with Lateral Epicondylitis

Lateral Epikondilitli Hastalarda Nöropatik Ağrının Sıklığı ve Özürlülüğe Etkisi

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ABSTRACT Objective: To evaluate the frequency of neuropathic pain and its effect on disability in patients with lateral epicondylitis (LE). **Material and Methods:** Eighty eight patients with LE over the age of 18 were invited to the study. Patients were grouped according to the presence of neuropathic pain using the PainDETECT Questionnaire (PDQ): 26 patients with score of ≥19 in neuropathic pain (NEP) group and 50 patients with score of ≤12 in nociceptive pain (NOP) group. Pain level was assessed by visual analogue scale (VAS) (VAS at first visit, worst and average VAS scores in last 4 weeks) and disability by Quick-Disability of Arm, Shoulder and Hand (Quick-DASH) Scale. **Results:** NEP was detected in 26 (29.5%) and NOP was detected in 50 (56.8%) patients with LE. VAS at the initial visit, worst VAS and average VAS scores during past 4 weeks were significantly higher in NEP group (p=0.003, p=0.006, p=0.004 respectively). Quick-DASH score was 64.62 (55.06-75) in NEP and 45.12 (28.93-52.81) in NOP groups (p<0.001). Positive correlations were found between VAS score at the initial visit, worst VAS and average VAS scores during the past 4 weeks and PDQ scores in NEP group (r=0.652 p<0.001, r=0.436 p=0.026, r=0.661 p<0.001 respectively). Quick-DASH score was found to be an independent prognostic factor for NEP (p=0.001). **Conclusion:** NEP may cause an increased disability in patients with LE, therefore it is necessary to evaluate NEP in this patient group.

Keywords: Lateral epicondylitis, neuropathic pain, disability

ÖZET Amaç: Bu çalışmada amaç, lateral epikondilitli (LE) hastalarda nöropatik ağrı sıklığının ve nöropatik ağrının özürlülüğe etkisinin değerlendirilmesidir. **Gereç ve Yöntemler:** Çalışmaya 18 yaş üstü LE'li 88 hasta davet edildi. Hastalar PainDETECT Ölçeği [PainDETECT Questionnaire (PDQ)] ile nöropatik ağrının varlığına göre gruplandırıldı: Nöropatik ağrı [neuropathic pain (NEP)] grubuna PDQ skoru ≥19 olan 26 hasta ve nosiseptif ağrı [nociceptive pain (NOP)] grubuna PDQ skoru ≤12 olan 50 hasta dâhil edildi. Ağrı düzeyi, görsel analog skalası [visual analogue scale (VAS)] (ilk vizitteki VAS, son 4 haftadaki en kötü ve ortalama VAS skoru) ile özürlülük Hızlı-Kol, Omuz ve El Sorunları [Quick-Disability of Arm, Shoulder and Hand (Quick-DASH)] Ölçeği ile değerlendirildi. **Bulgular:** LE'li hastaların 26'sında (%29,5) NEP, 50'sinde (%56,8) NOP saptandı. İlk vizitteki VAS, son 4 haftadaki en kötü VAS ve ortalama VAS skorları NEP grubunda anlamlı olarak daha yüksekti (sırasıyla p=0,003, p=0,006, p=0,004). Quick-DASH skoru NEP'de 64,62 (55,06-75), NOP gruplarında 45,12 (28,93-52,81) idi (p<0,001). NEP grubunda, ilk vizitteki VAS skoru, son 4 haftadaki en kötü VAS ve ortalama VAS skorları ile PDQ skorları arasında pozitif korelasyon bulundu (sırasıyla r=0,652 p<0,001, r=0,436 p=0,026, r=0,661 p<0,001). Quick-DASH skoru NEP için bağımsız prognostik faktörler olarak bulundu (p=0,001). **Sonuç:** NEP, LE hastalarda artmış özürlülüğe neden olabilir, bu nedenle bu hasta grubunda NEP'in değerlendirilmesi gereklidir.

Anahtar Kelimeler: Lateral epikondilit, nöropatik ağrı, özürlülük

Neuropathic pain (NEP) is a type of chronic pain caused by nerve damage that occurs in a path form the primary afferent nerve to the higher brain centers via spinal cord.[1] In general population, NEP prevalence may be as high as 7 to 8%, accounting for 20-25% of patients with chronic pain.[2-4] Diabetes mellitus, herpes zoster infection, nerve compression and autoimmune disease etc. can cause NEP. Central and peripheral sensitization mechanisms play a role in NEP.[5]

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Lateral epicondylitis (LE) is a common painful problem and seen in 1-3% of individuals. Although it often causes acute pain, it can become a chronic condition less frequently.[6,7] Perhaps the cause of chronic LE may be NEP and central sensitization. There are no studies evaluating the presence of NEP in LE, although there are some studies in the literature showing NEP in patients with shoulder tendon rupture/impingement syndrome and knee osteoarthritis.[8-11]

In this study, we aimed to evaluate the frequency of the NEP and its effect on disability in patients with LE.

MATERIAL AND METHODS

This study was planned as a cross sectional study. Eighty eight patients with LE for more than 1 month and over the age of 18 years were invited to the study. Patients were grouped according to the presence of NEP using the PainDETECT Questionnaire (PDQ): 26 patients with score of ≥19 in NEP group and 50 patients with score of ≤12 in nociceptive pain (NOP) group. Approval for the study was obtained from the Hitit University Faculty of Medicine Clinical Research Ethics Committee (date: March 11, 2020, no: 192). A well written informed consent was obtained from all participants according to the principles of the Helsinki Declaration.

The inclusion criteria were provocation of the lateral elbow pain with at least one of the following tests: 1) Resisted middle finger extension, 2) Resisted wrist extension, 3) Passive stretch of wrist entensors. Participants with concomitant rheumatic diseases, neurological diseases; history of other systemic diseases such as hypothyroidism/hyperthyroidism, diabetes mellitus; previous history of overt trauma, previous history of orthopedic surgery were excluded.

The demographic and clinical features were recorded. Pain level was assessed with visual analogue scale (VAS) (VAS at first visit, worst and average VAS scores in last 4 weeks) and the disability level was assessed with Quick-Disability of Arm, Shoulder and Hand (Quick-DASH) Scale.

VAS is used for measuring the pain level. The VAS consist of a 10 cm horizontal line with two ends labelled as 0 cm representing “no pain” and 10 cm the “worst pain”.[12,13]

Quick-DASH is a shorter version of the original DASH. This questionnaire contains 11 questions with five choices for each question. The final score can range 0 (best)-100 (worst).[14] Study results shows that the Quick-DASH can be used instead of the original DASH.[15,16] The validity and reliability of the Quick-DASH for Türkiye was assessed by Altan et al.[17]

The PDQ was used for NEP.[9,18] There are 9 questions in this questionnaire. A score of ≤12 indicates a high likehood of a nociceptive component and a score of 13-18 indicates the possibility of a neuropathic component. A score of ≥19 indicates NEP. The validity and reliability of the PDQ for Türkiye was assessed by Alkan et al.[19]

Number of patients was determined assuming a 6.5 mean difference and 2.1 standard deviation of points at VAS with 80% power and 5% significance.[8]

STATISTICAL ANALYSES

All data were analyzed using the SPSS (SPSS Inc., Chicago, IL, USA) 15.0 program for Windows. The variables were investigated using visual and analytical methods to determine whether or not they are normally distributed. Continuous variables are expressed as mean±standard deviation and categorical variables as numbers and percentages.

Student t-test was used to determine age, VAS at the initial visit, worst VAS score during past 4 weeks, average VAS score during the past 4 weeks and pain duration for comparing NEP and NOP groups. Mann-Whitney U test was used to determine PDQ and Quick-DASH scores for comparing NEP and NOP groups. Chi-square test was used for nominal values for comparing NEP and NOP groups. The univariate analyses to identify variables associated with patients outcome (presence of neurpathic pain/absence of NEP) was investigated chi-square and Student’s t-tests and Mann-Whitney U where appropriate. For the multivariate analyses, the possible factors identified with univariate analyses were further entered into the logistic regression analysis to determine independent predictors. Hosmer-Lemeshow goodness of fit statistics were used to assess model fit. Spearman

correlation coefficient was used to evaluate the linear relationship between predictive variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

The distribution of the patients according to the PDQ scores was as follows: 26 (29.5%) patients with score of ≥19 on PDQ in NEP group and 50 (56.8%) patients with score of ≤12 on PDQ in NOP group. Demographic and clinical features of all patients with LE were summarized in Table 1. Age, gender distribution and pain duration were similar between NEP and NOP groups (Table 2). VAS at the initial visit, worst VAS score during past 4 weeks and average VAS score during past 4 weeks, PDQ and Quick-DASH scores were significantly higher in NEP group (Table 2).

TABLE 1: Demographic and clinical features of all patients.

	All patients n=88
Age (year)	46.5±7.98
Gender, n (%)	31 (35.2) (male)
	57 (64.8) (female)
Dominant arm, n (%)	84 (95.5) (right)
Affected elbow, n (%)	55 (62.5) (right)
Pain duration (month)	5.57±4.97
VAS at the initial visit	7.12±1.65
Worst VAS score during past 4 weeks	7.96±1.27
Average VAS score during past 4 weeks	6.47±1.72

VAS: Visual analogue scale; Data are presented as mean±standard deviation, median (25-75%) or numbers and percentages; $p<0.05$.

Positive correlations were found between VAS score at the initial visit, worst VAS score during past 4 weeks, average VAS score during the past 4 weeks and PDQ scores in NEP group (Table 3). There were no correlations between age, pain duration, Quick-DASH and PDQ scores (Table 3). Quick-DASH score was found to be independent prognostic factors for NEP (Table 4).

DISCUSSION

To our knowledge, this is the first study to evaluate the presence of NEP in patients with LE. We found that 29.5% of patients with LE have NEP. We found a positive correlation between VAS score at the initial visit, worst VAS score during the past 4 weeks, average VAS score during the past 4 weeks and PDQ score in NEP group. Disability scores were found higher in NEP group. Also we found that disability score was a prognostic factor for NEP in LE patients.

NEP is characterized by spontaneous pain with abnormal sensory symptoms, such as persistent or paroxysmal pain and it contains some types of pain, such as hyperalgesia or allodynia.[18] There are several pathophysiological mechanisms involved in the peripheral and central nervous system for the generation of NEP.[5] In LE, some changes may occur in neurons in the peripheral nervous system because neurotransmitters released due to pain or chemicals released due to direct irritation, and ultimately may lead to sensitization of the central nervous system.[20] Substance P is a neuropeptide and it is commonly

TABLE 2: Demographic and clinical features of NEP and NOP groups.

	NEP group n=26	NOP group n=50	p value
Age (year)	45.61±7.20	48.64±8.50	0.126
Gender, n (%)	6 (23.1) (male)	20 (76.9) (female)	21 (42) (male)
29 (58) (female)	0.102		
Pain duration (month)	7.34±5.98	5.02±4.60	0.064
VAS at the initial visit	7.84±1.51	6.60±1.62	0.003
Worst VAS score during past 4 weeks	8.46±1.27	7.62±1.22	0.006
Average VAS score during past 4 weeks	7.19±2.03	6.0±1.45	0.004
Quick-DASH score	64.62 (55.06-75)	45.12 (28.93-52.81)	<0.001
PDQ score	23.5 (21-26.5)	8 (6-10.25)	<0.001

NEP: Neuropathic pain; NOP: Nociceptive pain; VAS: Visual analogue scale; DASH: Disability of Arm, Shoulder and Hand; PDQ: The PainDETECT Questionnaire; Data are presented as mean±standard deviation or median (25-75%); $p<0.05$.

TABLE 3: Correlation between PDQ score and age, VAS, pain duration and Quick-DASH score in NEP group.

	PDQ r value	PDQ p value
Age	0.155	0.448
Pain duration	0.059	0.774
VAS at the initial visit	0.652	<0.001
Worst VAS score during past 4 weeks	0.436	0.026
Average VAS score during past 4 weeks	0.661	<0.001
Quick-DASH score	0.271	0.180

PDQ: The PainDETECT Questionnaire; VAS: Visual analogue scale; DASH: Disability of Arm, Shoulder and Hand; NEP: Neuropathic pain.

TABLE 4: Clinical factors related with neuropathic pain using the multivariate analyses (logistic regression).

Independent factors	Exp	95% CI	p value
VAS at the initial visit	1.028	0.554-1.906	0.930
Worst VAS score during past 4 weeks	1.240	0.666-2.307	0.497
Average VAS score during past 4 weeks	1.022	0.638-1.638	0.927
Quick-DASH	1.087	1.036-1.140	0.001

p<0.05; CI: Confidence interval; VAS: Visual analogue scale; DASH: Disability of Arm, Shoulder and Hand.

found in the central and peripheral nervous system. There is some evidence that substance P plays a role not only in the nociceptive pathway but also in local neurogenic inflammation.[21-23] The primary receptor for substance P is the neurokinin 1 (NK1) receptor. Increased expression of NK1 receptors is known as a part of acute inflammation.[24] These receptors were shown in chronic painful tendon disease.[24] Peterson et al. examined 10 patients with LE by positron emission tomography. They showed increased expression of NK1 receptors in peripheral tissue.[25] This increased NK1 receptors have been interpreted as part of a process defined as neurogenic inflammation.[25] We found that 29.5% of patients with LE have NEP. Patients who had LE for more than one month were included in our study. The presence of NEP in patients with LE may due to increased NK1 receptors.

Studies investigating NEP in musculoskeletal diseases are limited except low back pain. Karasugi et al. found that 10.9% of patients with rotator cuff tears may have NEP. They included 110 patients with rotator cuff tears into their study.[8] They found that average pain during the past 4 weeks was a prognostic factor for NEP in patients with rotator cuff tears.[8] They did not find any relationship between pain duration and NEP. They thought that inflammation caused by rotator cuff tears may result from the injury of the neural mechanoreceptors and suprascapular nerve. So, rotator cuff tears may cause development of NEP.[8] Ko et al. found that 15.8% of patients with rotator cuff tears may have NEP.[26] Also they found that average VAS score during the past 4 weeks and rotator cuff tear size were prognostic factors for NEP in patients with rotator cuff tears.[26] We found that 29.52% of patients with LE have NEP. We did not find VAS score as a prognostic factor for NEP in patients with LE. Disability score was found as a prognostic factor in our study. Also we found a significant correlation between PDQ score and VAS score at the initial visit, worst VAS score during past 4 weeks and average VAS score during the past 4 weeks in LE patients with NEP.

Ohtori et al. investigated the prevalence of NEP in 92 patients with knee osteoarthritis and they found that 5.4% of patients had NEP and 15% had possible NEP.[10] They found a significant correlation between PDQ score and VAS scores (average pain during the past 4 weeks) in patients with knee osteoarthtiritis.[10] They did not find any associations between PDQ score, symptom duration and age. Similar to this study, we did not find any association between PDQ score, age and pain duration in LE patients with NEP. NEP may occur associated with damage to nerves innervating subchondral bone in knee osteoarthritis.[10] Polat et al. investigated the prevalence of NEP in 109 patients with knee osteoarthritis and they found 11% of patients had NEP, 21% of patients had possible NEP.[27] Also they found an association between PDQ score, VAS and Western Ontario and McMaster Universities osteoarthritis index (pain, physical function and total scores) scores.[27] Similar to this study, disability score was increased and VAS scores were associated with PDQ score in NEP group in our study.

This is the first study evaluating the presence of NEP in patients with LE in the literature. So, it will contribute to the literature in determining and improving the management of LE. We found that 29.5% of patients with LE have NEP by using the PDQ. Also we found that Quick-DASH score was a prognostic factor for NEP in patients with LE.

CONCLUSION

As a conclusion, patients with LE may have NEP. Disability score is an independent prognostic factor for NEP in patients with LE. NEP may cause an increased disability in patients with LE, therefore it is necessary to evaluate NEP in this patient group.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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